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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/009,956	04/12/2002	Mark Sanders	301.1003	3247

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EXAMINER	
GOLLAMUDI, SHARMILA S	
ART UNIT	**PAPER NUMBER**
1616	

DATE MAILED: 09/14/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/009,956	SANDERS, MARK	
	Examiner	Art Unit	
	Sharmila S. Gollamudi	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *6/25/04*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20,23-29,34,36 and 37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20,23-29,34,36 and 37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Receipt of Amendments, Remarks, and the Information Disclosure Statement received on June 25, 2004 is acknowledged. Claims **1-20, 23-29, 34, and 36-37** are pending in this application.

Response to Arguments

Applicant's arguments with respect have been considered but are moot in view of the new ground(s) of rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-20, 23-28 29 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of asthma and Chronic Obstructive Pulmonary Disease, it does not reasonably provide enablement for treating *all* respiratory disorders. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Enablement is considered in the view of the Wands factors (MPEP 2164.01 (a)). These include the nature of the claims, guidance of the specification, the existence of working examples, predictability of the prior art, and state of the prior art. All of the Wands factors have been considered with the regard to the instant claims, with the most relevant discussed below.

Nature of the Invention: The rejected claims are drawn to the method of treating or alleviating a respiratory disorder by administering an effective amount of formoterol and

fluticasone. The nature of the invention is extremely complex in that it encompasses treating and preventing all possible disorders related to the respiratory tract by treating it one composition.

Breath of the claims: The complex nature of the claims is greatly exacerbated by the breath of the claims. The claims encompass the treatment all respiratory disorders such as i.e. lung cancer, Adult and infant respiratory distress syndrome (ARDS and IRDS), the common cold, etc.

Guidance of the Specification: The guidance provided by the specification speaks on how to administer the composition to a subject in order to treat asthma and Chronic Obstructive Pulmonary Disease. However, the guidance provided is not directed to the actual treatment of *all* respiratory disorders, i.e. the specification is silent on other disorders related to the respiratory tract such as lung cancer, Adult and infant respiratory distress syndrome (ARDS and IRDS), the common cold, etc.

Working Examples: All of the working examples provided by the specification are directed towards the treatment of lung inflammation. The examples are silent on treatment and prevention of other diseases related to the respiratory tract.

Predictability of the Art: The lack of significant guidance from the specification or the prior art with regard on how to treat all lung disorders makes practicing this scope of the invention unpredictable since all respiratory diseases are not linked by one common cause to allow treatment it with one, highly specific composition.

The State of the Art: The state of the art does not link all respiratory disorders with one common cause, which allows treatment with one highly specific composition. For instance, the

state of the art provides that the common cold is not treated by the instant composition since steroids are known to suppress the immune system, hence prolonging the cold.

The Amount of experimentation Necessary: In order to practice the claimed invention, a skilled artisan would have to predict what respiratory disease may be treated by the instant composition, followed by predicting what the effective amount of the composition, if any, would treat each divergent respiratory disorder. If unsuccessful, which is likely given the lack of guidance form the specification and prior art, a skilled artisan would have experiment again. Therefore, the claimed scope would require undue and unpredictable experimentation to practice the instant invention in regards to treating all respiratory disorders.

Therefore, the claims are rejected under enablement. The examiner suggests limiting the claims to the treatment of asthma and Chronic Obstructive Pulmonary Disease.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 36-37 are rejected under 35 U.S.C. 102(b) as being anticipated by Carling et al (5,674,860).

Carling et al disclose a combination of a bronchodilator and a steroidal anti-inflammatory for the treatment of respirators diseases such as asthma. See abstract. Carling discloses that the long-term treatment of asthma with inhaled steroids has poor patient compliance whereas bronchodilators are readily taken. See column 1, lines 35-45. Carling states that bronchodilators

have short duration of action and by using a steroid, long-term treatment is provided. More specifically, Carling discloses the combination of formoterol and budesonide (glucocorticoid). Formoterol is an adrenorecptor agonist, which stimulates the beta-2 receptors and relaxes the smooth muscles and budesonide provides long term control of asthma. The combination not only provides a greater efficiency and duration of the bronchodilator i.e. the beta-2 receptor stimulating action, but the combination allows for a rapid onset. See column 2, lines 5-15.

Claims 36-37 are rejected under 35 U.S.C. 102(b) as being anticipated by Palmer (5,270,305).

Palmer discloses a composition containing salmeterol and fluticasone to treat asthma and other respiratory disorders. See column 1, lines 5-6. Asthma is treated using a bronchodilator for immediate relief and a prophylactic anti-inflammatory corticosteroid to treat underlying inflammation. Salmeterol is taught as a bronchodilator, a highly effective beta-2 receptor stimulant that relaxes the smooth muscles and fluticasone is taught as an anti-inflammatory corticosteroid. See column 1, lines 65-68. Palmer states that the novel combination of a steroid and bronchodilator has a markedly greater efficiency and duration of the bronchodilator action, i.e. the beta-2 receptor stimulating action. See column 1, lines 56-60.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-20, 23-29, 34, and 36-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ward (6,369,115) in view of Carling et al (5,674,860).

Ward teaches a stabilized dry powder formulation for the treatment of pulmonary conditions by using a first polar drug, a second non-polar drug, and a polar excipient. See abstract. Ward states that there is poor patient compliance for long-term treatment using inhaled steroids since they do not provide immediate relief for asthma. However, patients readily take bronchodilators since they provide rapid relief and the chance of overdosing is reduced. Ward further states that bronchodilators have a short duration of action, but with the use of a steroid, improved therapy is attained. See column 1. Ward teaches a composition containing fluticasone and fluticasone. See examples. The ratio of formoterol to fluticasone is within the range of 1;4 to 1:70. see column 2, lines 63-64.This dosing with a single dose inhaler provides for patient compliance. Ward teaches a dosage regimen of twice daily of formoterol in the range of 5-100mcg and fluticasone in the range of 10-100mcg. See column 2, line 65 to column 3, line 2. The preferred diluent or carrier is lactose. See column 2, line 20. The instant salt forms of formoterol are taught on column 2, lines51-62.

Ward does not teach the packaging of the medicaments as separate compositions. Further, although Ward teaches simultaneous/separate administration is not taught.

Carling et al teach a combination of a bronchodilator and a steroidal anti-inflammatory for the treatment of respirators diseases such as asthma. See abstract. Carling also teaches that the long-term treatment of asthma with inhaled steroids has poor patient compliance whereas bronchodilators are readily taken. See column 1, lines 35-45. Carling states that bronchodilators have short duration of action and by using a steroid, long-term treatment is provided. See column 2, lines5-15. The two actives may be administered simultaneously, sequentially, or separately depending on patient requirements. See column 2, lines 29-35. The suitable dose of formoterol is 6-100 micrograms twice a day. Formoterol is an adrenoceptor agonist, which selectively stimulates the beta-2 receptors, thus producing relaxation of the bronchial smooth muscles. See column 1, lines 46-50. However, the particular dose depends on the patient and severity of the disease. See column 3, lines 43-50. Carling teaches a combination of formoterol and budesonide. Carling further teaches optionally using a propellant mixture such as chlorofluorocarbon propellant 134, which suspends the drugs. The use of surfactants in a low concentration provides stability to the mixture. Carling teaches compositions with a surfactant stabilizer and without. See column 4, lines 1-15.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Ward and Carling et al and maintain medicament A in a separate reservoir from medicament B. One would be motivated to do so since Carling et al provide the state of the art wherein it is known and conventional in combination therapy of inhaled agents to combine the two medicaments to form one composition or maintain the two

medicaments separately since the criticality lies in the combination therapy of the bronchodilator and steroid and not in the packaging of the medicaments. Furthermore, the dosing of the medicaments either simultaneously, sequentially, or separately depends on patients parameters such as the severity of the condition and the treatment plan. Therefore, it is prima facie obvious to alter the packaging of a medicament in the desired fashion absent unexpected results.

Claims 11-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Palmer (5,270,305) in view of Carling et al (5,674,860) in further in view of WO 97/47286.

As set forth above, Ward teaches a composition containing formoterol and fluticasone to treat asthma and other respiratory disorders. Carling et al teach a combination of a bronchodilator and a steroidal anti-inflammatory for the treatment of respirators diseases such as asthma in a separate, sequential, or simultaneous administration. Carling teaches the use of HFA propellants.

The references do not teach the all of the instant propellant.

WO teaches a medicinal aerosol formulation of formoterol. The reference teaches the undesirability CFCs the environment and HFAs are viewed as more ozone friendly. Further, HFAs have low toxicity and vapor pressures suitable for use in aerosols. See page1, lines 13-18. Furthermore, the instant HFA 227 and HFA 134 provide a stable propellant system and HFA 227 is beneficial to producing homogenous suspensions. See page 3 and 5.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine Ward, Carling et al, and WO and utilize the instant propellant. One would be motivated to do so since WO teaches the advantages that the instant propellant system

provides. Therefore, one would be motivated to use HFA to provide a stable propellant system and a homogenous suspension of the drug and propellant.

Claims 1-20, 23-29, 34, and 36-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Clarke et al (PGPUB US 2002/0103260) in view of Hassan et al (6,537,524).

Clarke et al teach a combination of formoterol and fluticasone for treating inflammatory or obstructive diseases (COPD, COAD, COLD). See abstract and paragraph 0022. The combination allows for rapid onset and the reduction of unwanted side effects. See paragraph 0003. The administration of the composition is via an inhalable form such as nebulizers or aerosols. Clarke teaches the instantly claimed propellants, HFA 134, HFA 227, for the aerosol forms. The composition may also contain lubricants or surfactants or may include surfactant-free compositions. See paragraph 0011. The inhalable form may also be a dry powder form containing a conventional carrier such as instantly claimed lactose, which is the preferred carrier. See paragraph 0012 and examples. The weight ratio of formoterol to fluticasone is taught on paragraph 0016, which falls into instantly claimed range of 1:0.4 to 1:167. Instant salt forms are taught on Paragraph 0009. The suitable daily dosage of formoterol is in the range of 1-72 micrograms and for fluticasone it is in the range of 25-3000 micrograms. See paragraph 0017. Further, the composition may be administered twice a day.

Clarke et al do not teach the packaging of the medicaments as separate compositions.

Hassan et al teach a combination of formoterol and tiotropium salt for simultaneous, sequential, or separate administration in the treatment of inflammatory or obstructive airways diseases. See abstract. The combination allows for rapid onset and the reduction of unwanted

side effects. See column 1, lines 25-40. Hassan teaches the instantly claimed propellants, HFA 134, HFA 227, for the aerosol forms. The composition may also contain lubricants or surfactants or may include surfactant-free compositions. See column 2, lines 45-67. The inhalable form may also be a dry powder form containing a conventional carrier such as instantly claimed lactose, which is the preferred carrier. See column 3, lines 5-20. Hassan teaches the inhalable medicament may be administered using a pack using two or more inhalation devices. This kit comprises medicament A and B in separate devices or a single device containing medicament A and B in separate reservoirs of a multidose inhaler. See column 5, lines 23-40.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Clarke et al and Hassan et al and maintain medicament A in a separate reservoir from medicament B. One would be motivated to do so since Hassan et al provide the state of the art wherein it is known and conventional in combination therapy of inhaled agents to combine the two medicaments to form one composition or maintain two medicaments in separate reservoirs since the criticality lies in the combination therapy of the bronchodilator and steroid and not in the packaging of the medicaments. Furthermore, one would expect similar results since Hassan teaches that regardless of the packaging of the medicaments, they can be administered as desired sequentially, separately, or simultaneously, just as Clarke's medicaments are administered. Therefore, it is prima facie obvious to alter the packaging of a medicament.

Conclusion

No claims are allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharmila S. Gollamudi whose telephone number is 571-272-0614. The examiner can normally be reached on M-F (8:00-5:30), alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on 571-272-0887. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Sharmila S. Gollamudi
Examiner
Art Unit 1616

SSG

MICHAEL G. HARTLEY
PRIMARY EXAMINER